

Amendments to the Claims

Please cancel Claims 1-45. Please add new Claims 46-74. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

Claims 1-45 (Canceled)

46. (New) A method of screening for a compound that increases bone mass in a host at least 10% without a loss in bone strength or quality, comprising:
- (a) determining that the compound includes the following characteristics:
 - (i) binds to an estrogen α or β like receptor with an association constant of at least 10^8 M^{-1} ;
 - (ii)(a) induces estrogenic gene transcriptional activity at a level that is no greater than 10% that of 17β -estradiol when administered *in vivo* at concentrations of 10^{-11} to 10^{-7} M and at a dosage of at least 0.1 ng/kg body weight or *in vitro* in osteoblastic or osteocytic cells with estrogen receptors or (b) induces an increase in uterine weight of no more than 10% that of 17β -estradiol or analogs thereof;
 - (iii) induces the phosphorylation of extracellular signal regulated kinase (ERK) when administered *in vivo* at a dosage of at least 0.1 ng/kg body weight or *in vitro* at concentrations of 10^{-11} to 10^{-7} M in osteoblastic cells with estrogen receptors; and
 - (iv) has an anti-apoptotic effect on osteoblasts at an *in vivo* dosage of at least 0.1 ng/kg body weight or *in vitro* in osteoblastic or osteocytic cells with natural estrogen receptors or cells transfected with estrogen receptors; and
 - (b) selecting said compound including said characteristics.

47. (New) The method of Claim 46, wherein determining that the compound binds to an estrogen α or β like receptor with an association constant of at least 10^8 M^{-1} comprises: contacting the compound with an estrogen receptor from the host and measuring the association constant.
48. (New) The method of Claim 47, wherein the association constant of is measured by a competitive radiometric binding assay, comprising:
- a) contacting the compound with a sample comprising estrogen receptors and [^3H] estradiol,
 - b) incubating at room temperature or overnight at 4°C , allowing the binding of the compound to the receptor;
 - c) isolating bound receptor; and
 - d) comparing the amount of bound receptor displaced by the compound to a control sample of estrogen receptors with [^3H] estradiol to determine the association constant.
49. (New) The method of Claim 46, wherein the compound binds with an association constant of at least 10^{10} M^{-1} .
50. (New) The method of Claim 46, wherein determining that the compound induces estrogenic gene transcriptional activity at a level that is no greater than 10% that of 17β -estradiol when administered *in vivo* at concentrations of 10^{-11} to 10^{-7} M and at a dosage of at least 0.1 ng/kg body weight comprises: administering the compound to a host and monitoring the level of induction or suppression of a surrogate marker of estrogenic transcriptional activity.
51. (New) The method of Claim 50, wherein the surrogate marker of is selected from the group consisting of: complement C3 gene, lactoferin, IL-6 and a minimal gene containing one or more copies of the ERE driving a reporter gene.

52. (New) The method of Claim 46, wherein determining that the compound induces estrogenic gene transcriptional activity at a level that is no greater than 10% that of 17 β -estradiol when administered *in vitro* at concentrations of 10⁻¹¹ to 10⁻⁷ M and at a dosage of at least 0.1 ng/kg body weight includes: contacting the compound with cells having estrogen receptors and monitoring the level of induction or suppression of a surrogate marker.
53. (New) The method of Claim 52, wherein the surrogate marker of is selected from the group consisting of: complement C3 gene, lactoferin, IL-6 and a minimal gene containing one or more copies of the ERE driving a reporter gene.
54. (New) The method of Claim 53, wherein the cells of are selected from the group consisting of: human uterine HeLa cells, human embryonic kidney cells 293, murine osteocytic MLO-Y4 cells and murine osteoblastic calvaria derived cells.
55. (New) The method of Claim 46, wherein the determining of uterine weight increase includes ultrasound.
56. (New) The method of Claim 46, wherein the determining of uterine weight increase includes removing the uterus, weighing the uterus and comparing uterine weight to total body weight.
57. (New) The method of Claim 46, wherein determining the induction of the phosphorylation of extracellular signal regulated kinase (ERK) when administered *in vivo* at a dosage of at least 0.1 ng/kg body weight includes administering the compound to the host and measuring the increase of phosphorylation of ERK.
58. (New) The method of Claim 46, wherein determining the induction of the phosphorylation of extracellular signal regulated kinase (ERK) when administered *in*

vitro includes: contacting the cells with the compound, incubating the cells, quantitating phosphorylated ERK and comparing the amount of phosphorylated ERK with total ERK.

59. (New) The method of Claim 46, wherein the determining of anti-apoptotic effect includes: contacting osteoblasts or osteocytes from the host with a proapoptotic agent both alone and in combination with the compound; and measuring the inhibition of apoptosis; and comparing apoptosis where a decrease in apoptosis the presence of compound indicates an anti-apoptotic effect.
60. (New) The method of Claim 46, further comprising determining the compound does not induce estrous and does not induce significant androgenic gene transcriptional activity.
61. (New) A method of screening for a compound that increases bone mass in a host at least 10% without a loss in bone strength or quality, comprising:
 - (a) determining that the compound includes the following characteristics:
 - (i) binds to an androgen like receptor with an association constant of at least 10^8 M^{-1} ;
 - (ii)(a) induces androgenic gene transcriptional activity at a level that is no greater than 10% that of testosterone when administered *in vivo* at concentrations of 10^{-11} to 10^{-7} M at dosage of at least 0.1 ng/kg body weight or *in vitro* in osteoblastic or osteocytic cells with androgen receptors or (b) induces an increase in muscle weight or virilization in the host of no more than 10% that of testosterone and analogs thereof;
 - (iii) induces the phosphorylation of extracellular signal regulated kinase (ERK) when administered *in vivo* at a dosage of at least 0.1 ng/kg body weight or *in vitro* at concentrations of 10^{-11} to 10^{-7} M in osteoblastic cells of the host with androgen receptors; and
 - (iv) has an anti-apoptotic effect on osteoblasts at an *in vivo* dosage of at least 0.1 ng/kg body weight or *in vitro* in osteoblastic or osteocytic cells from the host with androgen receptors; and

(b) selecting said compound having said characteristics.

62. (New) The method of Claim 61, wherein determining the association constant includes contacting the compound with an androgen receptor of the host and measure the association constant.
63. (New) The method of Claim 61, wherein the association constant is measured by a competitive radiometric binding assay, comprising:
 - a) contacting the compound with a sample from the host comprising androgen receptors and [^3H] synthetic androgen RU1881;
 - b) incubating to allow binding of the compound to the receptor;
 - c) isolating bound receptor; and
 - d) comparing the amount of bound receptor displaced by the compound to a control sample of androgen receptors with [^3H] synthetic androgen RU1881 to determine the association constant.
64. (New) The method of Claim 61, wherein determining that the compound induces androgenic gene transcriptional activity *in vivo* comprises: administering the compound to a host and monitoring the level of induction or suppression of a surrogate marker of androgenic transcriptional activity.
65. (New) The method of Claim 64, wherein the surrogate marker is prostate specific antigen.
66. (New) The method of Claim 61, wherein determining that the compound induces androgenic gene transcriptional activity *in vitro* comprises: contacting the compound with a cell of the host having androgen receptors and monitoring the level of induction or suppression of a surrogate marker.
67. (New) The method of Claim 66, wherein the androgen induced transcriptional activity is assessed in cells selected from the group consisting of: osteoblastic cells with natural

androgen receptors, osteocytic cells with natural androgen receptors, rat calvaria cells, ML0-Y4 osteocytic cells and HeLa cells.

68. (New) The method of Claim 66, wherein the surrogate marker is prostate specific antigen.
69. (New) The method of Claim 61, wherein the phosphorylation is assessed in biopsies from the host using immunohistostaining with specific antibodies against phosphorylated ERKs.
70. (New) The method of Claim 69, wherein the biopsy is from bone.
71. (New) A method of screening for compounds that possess bone anabolic effects, comprising:
 - a) contacting a sample of osteoblast cells with a compound; and
 - b) comparing the number of osteoblast cells undergoing apoptosis in the compound-treated cells with the number of osteoblast cells undergoing apoptosis in an untreated same of osteoblast cells,wherein a lower number of apoptotic cells following contact with the compound indicated that the compound possesses bone anabolic effects.
72. (New) The method of Claim 71, wherein apoptosis is determined by nuclear morphologic criteria, DNA end-labeling, DNA fragmentation analysis or immunohistochemical analysis.
73. (New) A method of screening for compounds that possess bone anabolic effects, comprising:
 - a) contacting a sample of osteocyte cells with a compound; and
 - b) comparing the number of osteocyte cells undergoing apoptosis in the compound-treated cells with the number of osteocyte cells undergoing apoptosis in an untreated same of osteocyte cells,

wherein a lower number of apoptotic cells following contact with the compound indicated that the compound possesses bone anabolic effects.

74. (New) The method of Claim 73, wherein apoptosis is determined by nuclear morphologic criteria, DNA end-labeling, DNA fragmentation analysis or immunohistochemical analysis.